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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/540,212	01/12/2006	Jose Maria Mato De La Paz	4258-112	5253
23448	7590	10/16/2006	EXAMINER	
INTELLECTUAL PROPERTY / TECHNOLOGY LAW			YANG, NELSON C	
PO BOX 14329			ART UNIT	PAPER NUMBER
RESEARCH TRIANGLE PARK, NC 27709			1641	

DATE MAILED: 10/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/540,212	MATO DE LA PAZ ET AL.	
	Examiner	Art Unit	
	Nelson Yang	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 11 July 2006.
- 2a) This action is **FINAL**. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-16 is/are pending in the application.
 - 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-16 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>9/14/05</u> . | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

1. Applicant's amendment has rendered the previous restriction requirement moot, and therefore the restriction with respect to claims 1-16 mailed June 12, 2006 has been withdrawn.
2. Claims 1-16 are currently pending.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.
4. Claims 1-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
5. Claim 1 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the steps that recite how one of ordinary skill in the art would make the diagnosis of whether a subject had or was susceptible to NASH based on the comparison of the results with normal reference values. As applicant themselves have disclosed, the markers recited in claims 1-16 are also known markers for a variety of other symptoms and diseases, such as inflammation, hepatic carcinoma, chronic hepatitis, alcoholic steatohepatitis and cirrhosis (see p. 6). Furthermore, by merely comparing the results of step a) with normal reference values for said proteins in liver tissue would not allow one of ordinary skill in the art to make the determination of the presence of or susceptibility to NASH in a subject, as the claim

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recites. In order to do this, one of ordinary skill in the art would further need to know the levels of the different markers, relative to reference values, that would allow one to make the diagnosis that a subject had NASH, and to distinguish a subject with NASH from a subject with another disease, such as inflammation, hepatic carcinoma, chronic hepatitis, alcoholic steatohepatitis and cirrhosis. Furthermore, from the specification itself, applicants appear to require measurement of at least two different markers (see p.11), wherein if the measurement of a marker selected from APA1, ATPB, LKHA K1CR, GAMT, SODC, ALBU, and AOP2 is higher than normal, and the measurement of the second marker selected from PHB1, MAT, ACDL, SBP is lower than normal, then the diagnosis of presence of or susceptibility to NASH may be made.

6. Claims 14-15 provide for the use of a protein, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

7. The remaining claims are indefinite due to their dependence on an indefinite claim.

Claim Rejections - 35 USC § 101

8. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

9. Claims 14-15 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for

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example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

11. Claims 1-7, 9, 10 are rejected under 35 U.S.C. 102(e) as being anticipated by Rose et al. [US 2006/0084067].

12. With respect to claim 16, Rose et al. teach the evaluation of different markers such as manganese superoxide dismutase and apoA1 (para. 0122) by comparing the levels of the markers in an individual to a cut off value (reference values) to determine whether the individual is positive for the marker (para. 0025). Therefore, since Rose et al. teach all the steps recited in the claim, the method of Rose et al. would anticipate the instant claim.

13. With respect to claim 1, the sample may be liver tissue (para. 0012).

14. With respect to claim 2, the sample is from an individual who is human (para. 0102).

15. With respect to claims 6, 7, 9, 10, Rose et al. teach the evaluation of different markers such as manganese superoxide dismutase and apoA1 (para. 0122).

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16. With respect to claims 3, 4, Rose et al. teach the use of antibodies to detect the markers (para. 0105).

17. With respect to claim 5, Rose et al. teach that Western blots may be used to detect the markers (para. 0114).

18. Claims 1-4 rejected under 35 U.S.C. 102(a) as being anticipated by Santamaria et al. [Santamaria et al., Functional proteomics of nonalcoholic steatohepatitis : mitochondrial proteins as targets of S-adenosylmethionine, March 2003, PNAS, 100(6), p.3065-3070].

Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

19. With respect to claims 1, 16, Santamaria et al. teach the observation of changes in expression pattern of proteins and identify antioxidant protein 2, superoxide dismutase, apolipoprotein A1, leukotriene A4 hydrolase, keratin type 1 cytoskeletal 18, guanidinoacetate methyltransferase, prohibitin 1, ACDL and ATPase β -subunit as markers of nonalcoholic steatohepatitis (p.3068, cols 1-2), by comparing the levels with those in control livers (p.3069, col.1).

20. With respect to claim 2, Santamaria et al. take samples from obese patients (human being) (p.3069, col.1).

21. With respect to claims 3-4, Santamaria et al. teach the use of antibodies for prohibitin, ATP synthase β -subunit (p.3066, col.1).

22. With respect to claim 5, Santamaria et al. teach the use of Western Blot analysis (p.3066, col.2).

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23. With respect to claims 5-7, 9-13, Santamaria et al. teach the observation of changes in expression pattern of proteins and identify antioxidant protein 2, superoxide dismutase, apolipoprotein A1, leukotriene A4 hydrolase, keratin type 1 cytoskeletal 18, guanidinoacetate methyltransferase, prohibitin 1, ACDL and ATPase β -subunit as markers of nonalcoholic steatohepatitis (p.3068, cols 1-2), by comparing the levels with those in control livers (p.3069, col.1).

24. With respect to claim 8, Santamaria et al. teach that down-regulation of PHB1 is found in the liver of obese patients compared to controls (p.3069, col.1), and that apolipoprotein A1 is up-regulated (p.3068, col.1).

Conclusion

25. No claims are allowed.

26. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nelson Yang whose telephone number is (571) 272-0826. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571)272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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27. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nelson Yang
Patent Examiner
Art Unit 1641

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LONG V. LE 09/29/06
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